APPENDIX D. Calculations

Calculation Equations:

1. Conversion of ppm to amortized daily dose (mg/kg/day):

$$\text{ppm x } 4.17\ \text{mg} / \text{m}^3 \text{ x inhalation rate x } \frac{\text{hours exposed}}{24\ \text{hours}} \text{ x } \frac{\text{days exposed}}{7\ \text{days}} \text{ x AF}$$

The term for number of days exposed /7 days is used in the calculation only for studies when the animals were dosed for 5 or more days. The default inhalation rates used are: 0.96 m^3/kg/day for rats and 0.54 m^3/kg/day for rabbits (Zielhuis and van der Kreek, 1979). An absorption factor (AF) of 18% is applied only to the critical NOELs when they are used to calculate the margins of exposure.

2. Dosage calculation for acute critical NOEL of 300 ppm in rats (Albee *et al*., 1993a).

$$300\ \text{ppm x } 4.17\ \text{mg} / \text{m}^3 \text{ x } 0.96\ \text{m}^3 / \text{kg} / \text{day x } \frac{6\ \text{hours exposed}}{24\ \text{hours}} = 300\ \text{mg} / \text{kg} / \text{day}$$

Absorbed dosage= 300 mg/kg/day x 0.18= 54 mg/kg/day

3. Dosage calculation for 1-2 week critical NOEL of 100 ppm in rabbits (Eisenbrandt *et al*., 1985).

$$100\ \text{ppm x } 4.17\ \text{mg} / \text{m}^3 \text{ x } 0.54\ \text{m}^3 / \text{kg} / \text{day x } \frac{6\ \text{hours exposed}}{24\ \text{hours}} \text{ x } \frac{5\ \text{days}}{7\ \text{days}} = 40\ \text{mg} / \text{kg} / \text{day}$$

Absorbed dosage= 40 mg/kg/day x 0.18= 7.2 mg/kg/day

4. Dosage calculation for subchronic critical NOEL of 30 ppm in rabbits (Nitschke *et al*., 1987b).

$$30\ \text{ppm x } 4.17\ \text{mg} / \text{m}^3 \text{ x } 0.54\ \text{m}^3 / \text{kg} / \text{day x } \frac{6\ \text{hours exposed}}{24\ \text{hours}} \text{ x } \frac{5\ \text{days}}{7\ \text{days}} = 12\ \text{mg} / \text{kg} / \text{day}$$

Absorbed dosage= 12 mg/kg/day x 0.18= 2.2 mg/kg/day

5. Dosage calculation for chronic critical NOEL of 5 ppm in rats (Breslin *et al*., 1992; Quast *et al*., 1993a).

$$5 \text{ ppm} \times 4.17 \text{ mg}/\text{m}^3 \times 0.96 \text{ m}^3/\text{kg}/\text{day} \times \frac{6 \text{ hours exposed}}{24 \text{ hours}} \times \frac{5 \text{ days}}{7 \text{ days}} = 4 \text{ mg}/\text{kg}/\text{day}$$

Absorbed dosage= 4 mg/kg/day x 0.18= 0.72 mg/kg/day

6. Margin of Exposure:

$$\frac{\text{NOEL (mg/kg/day)}}{\text{Human Exposure (mg/kg/day)}} = \text{Margin of Exposure}$$

7. Calculation of Reference Concentration in ppm:

The reference concentration in ppm is calculated by first determining the human equivalent NOELs by the following equation. The default adult and child inhalation rates (IR) are 0.28 m^3/kg/day and 0.59 m^3/kg/day, respectively. For acute exposure, there is no amortization of the number of days exposed. The interspecies extrapolation factor of 10 is retained because this equation only addresses the differences in the inhalation rate between animals and human and not other physiological factors. The total uncertainty factor may be 100 for interspecies extrapolation and intraspecies variation, or 1000 with an additional 10-fold factor for database uncertainty for developmental neurotoxicity. The uncertainty factor of 1000 was applied to reference concentrations for residential (children) exposures.

$$\text{Animal NOEL ppm} \times \frac{\text{animal IR}}{\text{human IR}} \times \frac{\text{hours exposed}}{24 \text{ hours}} \times \frac{\text{days exposed}}{7 \text{ days}} = \text{Human equivalent NOEL ppm}$$

$$\text{Human equivalent NOEL in ppm} \times 4.17 \text{ mg}/\text{m}^3/\text{ppm} = \text{Human NOEL in mg}/\text{m}^3$$

$$\frac{\text{Human NOEL as ppm or mg/m}^3}{\text{Uncertainty Factor of 100 or 1000}} = \text{Reference Concentration}$$

The following is an example of the calculation using the child inhalation rate and the acute NOEL of 300 ppm:

$$300 \text{ ppm} \times \frac{0.96 \text{ m}^3/\text{kg}/\text{day}}{0.59 \text{ m}^3/\text{kg}/\text{day}} \times \frac{6 \text{ hours exposed}}{24 \text{ hours}} = 122 \text{ ppm}$$

$$\frac{122 \text{ ppm}}{1000} = 0.122 \text{ ppm or } 0.51 \text{ mg}/\text{m}^3$$